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**Remarks**

Upon entry of the amendment, claims 1, 3, 5-9, 11-14, 20-22, 27, and 54-62 will be pending in the application. Claims 2, 3, 4, 10, and 11 have been cancelled. Support for the amendment to claim 1 appears in, e.g., original claims 2, 3, 4, 10, 11, and FIG. 6. Claim 20 has been amended to clarify the recitation of "GP Iba". New claims 54-59 are supported by, e.g., original claim 3. New claims 60-62 are supported by original claims 1, 2, 4, 7, 10, and 11. Claims 23-26 and 28-53 are cancelled as drawn to non-elected subject matter. Applicants reserve the right to pursue the subject matter of all cancelled claims in a continuing application or applications.

The examiner objected to claim 7 for the spelling of "von Willebrand" factor. The claim has been amended as suggested by the Examiner.

The objection to the specification as failing to provide proper antecedent basis for the claimed subject matter is moot in view of the amendments to claim 6 and claim 9.

**Rejection under 35 USC 112, first paragraph**

Claims 1-4, 6-19, 21-22 and 27 are rejected for overbreadth and for lack of written description. These rejections are traversed to the extent they are applied to the claims as amended.

Claim 1, from which the remaining claims subject to the rejection depend, has been amended to incorporate the subject matter of now cancelled claims 2, 4, 7, 10, and 11. As amended claim 1 is drawn to a fusion polypeptide that includes a first polypeptide

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11. As amended claim 1 is drawn to a fusion polypeptide that includes a first polypeptide operably linked to a second polypeptide. The first polypeptide includes a polypeptide sequence with at least 85% homology to an extracellular portion of a glycoprotein Iba polypeptide of SEQ ID NO: 1. Thus, the claim encompasses only those polypeptides having specified structural features--at least 85% homology to the extracellular portion of SEQ ID NO:1 and a specified function--binding to at least one of the four recited polypeptides leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin, or P-selectin.

New claim 59 corresponds to amended claim 1 except that it additionally requires that the first polypeptide consist essentially of a polypeptide sequence with at least 85% homology to the extracellular portion of a glycoprotein Iba polypeptide of SEQ ID NO:1 and that binds to vWF, and that the second polypeptide consist essentially of an immunoglobulin heavy chain polypeptide.

Methods for making polypeptides falling within the scope of the claims are known in the art and are additionally discussed at, e.g., page 7, lines 10-24 and page 12-30. Methods for detecting binding of a GP Iba protein to a ligand such as those recited in claim 1 are also well known in the art (see, e.g., Simon et al., J. Exp. Med. 192:193-204, 200, cited by Applicants at page 25, lines 30-32). Thus, one of ordinary skill in the art can readily practice the full scope of the invention now claimed.

The specification further makes clear that Applicants were in full possession of the invention now claimed when they filed the application. Glycoprotein Iba fusion polypeptides are discussed in detail in the specification at, e.g., page 6, line 6 to page 14,

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line 20. Moreover, the specification discloses six examples of polypeptides falling within the scope of the claims (SEQ ID NOs: 1-6).

In view of the foregoing comments, Applicants request reconsideration and withdrawal of the rejections for overbreadth and lack of written description.

Rejections under 35 USC 103(a)

Claims 1-5, 10-22 and 27 as being unpatentable over Lopez et al., (Proc. Natl. Acad. Sci. USA, 84:5615-19, 1987; hereinafter, "Lopez") in view of U.S. Patent No. 6,277,975 (hereinafter, "the '975 patent"). The rejection is traversed to the extent it is applied to the claims as amended.

Claims 2, 4, 10, 11, and 20 have been cancelled. Claim 1, from which the remaining claims subject to the rejection depend, has been amended so that it is drawn to a fusion polypeptide that includes a first polypeptide operably linked to a second polypeptide. The first polypeptide includes a polypeptide sequence with at least 85% homology to an extracellular portion of a glycoprotein Iba polypeptide of SEQ ID NO: 1. The claim additionally requires that the polypeptide binds to one of four polypeptides recited in claim 1.

The Examiner has the initial burden of establishing that the teachings of the applied art would have suggested the claimed invention to one of ordinary skill in the art and that such person would have had reasonable expectation of success. In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). However, this suggestion must be in the prior art and not in the Applicants' disclosure. In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

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With the instant rejection, the Examiner has improperly relied on Applicants' specification to find motivation for combining the references. Applicants teach in their specification that the claimed glycoprotein-Ib $\alpha$ -derived fusion proteins are useful for treating vascular conditions associated with vascular inflammation, including thrombosis, atherosclerosis, and angioplasty-related restenosis (page 2, lines 7-9). They further teach that the second polypeptide of the fusion protein can enhance the half-life (including the serum half-life) of the fusion protein (see page 10, lines 12-13). Thus, a motivation for making the claimed the claimed invention is to enhance the antiinflammatory effects of the glycoprotein-Ib $\alpha$  by adding the second polypeptide.

Motivation for making the claimed invention is absent in the applied art. Lopez provides a general review of the properties of glycoprotein Iba and describes the cloning of a human glycoprotein Iba cDNA. However, this reference says nothing about its therapeutic usefulness in treating vascular associated inflammation, let alone the therapeutic usefulness of an extracellular portion of the glycoprotein Iba when present in a fusion protein.

The secondary reference, the '975 patent fails to overcome the deficiencies of Lopez. The '975 patent is completely silent about glycoprotein Ib $\alpha$ , or about therapeutic uses of a fusion protein that includes all or part of glycoprotein Ib $\alpha$ . In short, there is no teaching in the applied references as to why one of ordinary skill in the art would combine them to arrive at Applicants' claimed invention. Rather, the only apparent reason discernible for combining the prior art of record is the Applicant's disclosure. Thus, the Examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention is obvious over Lopez in view of the '975 patent. In re Fritsch,

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972 F.2d 1260, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992); W.L. Gore Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983) cert. denied 469 U.S. 851 (1984) ("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher").

Claims 1-4, 6-19, 21-22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura *et al.*, J. Biol. Chem., 275:7539-46, 2000 (hereinafter, "Miura") in view of the '975 patent. The rejection is traversed to the extent it is applied to the claims as amended.

As noted above, claim 1, from which the remaining claims subject to the rejection depend, has been amended so that it is drawn to a fusion polypeptide that includes a first polypeptide operably linked to a second polypeptide. The first polypeptide includes a polypeptide sequence with at least 85% homology to an extracellular portion of a glycoprotein Iba polypeptide of SEQ ID NO: 1. The claim additionally requires that the polypeptide binds to one of four recited polypeptides--leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin, or P-selectin.

Miura is cited for describing a GPIb $\alpha$  calmodulin fusion protein and GPIb $\alpha$  calmodulin fusion proteins that include Iba233V, Iba239V, and Iba233V239V variant sequences; the latter corresponds to GPIb $\alpha$  sequences present in SEQ ID NO:5. Miura additionally reports that calmodulin was used in the fusion protein because it bound to the phenothiazine derivative W-7 agarose (see page 7541, first full paragraph and page 7540, third full paragraph). However, there is no teaching in Miura that a GPIb $\alpha$ -derived

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fusion protein is useful for treating vascular-associated inflammation, nor is there any suggestion in this reference for making a GPIIb $\alpha$ -derived fusion protein for any purpose other than to facilitate subsequent purification for *in vitro* biochemical binding studies. Thus, the combination of Miura and the '975 patent also produces the claimed invention only through impermissible hind-sight reconstruction.

Claims 1, 5 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura in view of the '975 patent and further in view of U.S. Patent No. 5,340,727 (hereinafter, "the '727 patent").

The non-obviousness of claim 1, from which depends claims 5 and 20, has been discussed above in view of the combination of Miura and the '975 patent. The '727 patent is cited for describing a 16 amino acid signal peptide with the sequence MPLLLLLLLPSLIP, which is present in the amino acid sequence of the protein sequences disclosed in Applicants' specification as SEQ ID NO: 1 and SEQ ID NO:5. However, the Examiner points to no motivation or suggestion in this reference for producing the invention of claim 1. Thus, the '727 patent fails to overcome the deficiencies of Miura and the '975 patent.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejections for obviousness.

### CONCLUSION

Applicants submit that the application is in condition for allowance, and such action is respectfully requested. Should any questions or issues arise concerning the

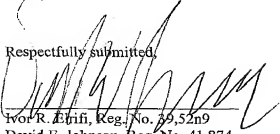
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application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

The Commissioner is authorized to charge payment of any fees required in connection with the papers transmitted herewith, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 22058-503).

Respectfully submitted,

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